Section: Anaesthesia

Original Research Article

COMPARISON OF INFUSION DEXMEDETOMIDINE WITH MAGNESIUM SULPHATE FOR ATTENUATION OF THE HAEMODYNAMIC RESPONSE DURING ENDOTRACHEAL INTUBATION IN ADULT PATIENTS

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Received : 08/08/2022
Received in revised form : 11/09/2022
Accepted : 25/09/2022

Keywords:
Airway, laryngoscopy response, dexmedetomidine, magnesium sulphate, haemodynamic parameters, sedation.

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DOI: 10.47009/jamp.2023.5.2.315

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 1505-1512

Abstract

Background: Laryngoscopy associated with increased circulating catecholamine leading to hemodynamic and cardiovascular responses. Many prophylactic drugs & methods have been used to alleviate the cardiovascular response to laryngoscopy & intubation. Aim of this study is to compare effectiveness of Dexmedetomidine 1µg/kg and Magnesium sulphate 50 mg/kg in attenuating cardiovascular response during laryngoscopy and intubation. **Materials and Methods:** 156 adult consented patients from ASA grade I & II, of either sex were included in study and randomly allocated into three groups. Group D received Dexmedetomidine 1µg/kg, Group M received Magnesium sulphate 50 mg/Kg & Group C received normal saline, over 10 minutes before induction & haemodynamic parameters were noted till 10 min after intubation. Two tailed unpaired t test used for comparison between groups & p value < 0.05 was considered as statically significant. **Result:** Patient's demographic data, characteristics & surgical procedure were comparable between three groups. There was significant increase in heart rate, systolic blood pressure, diastolic blood pressure & mean blood pressure after intubation in groups C & M as compared to group D. Hypotension was seen in six patients of each group D & M and in three patients of group C. Bradycardia was seen in one patient of each group D & M. **Conclusion:** Dexmedetomidine is better drug for attenuation of haemodynamic response to laryngoscopy & intubation, as compare to magnesium sulphate. Dexmedetomidine also produces more sedation which resembles normal sleep & thus leads to an anxiolytic effect on patients, as compared to magnesium sulphate.

INTRODUCTION

Laryngoscopy is an invasive stimulus during endotracheal intubation.[1,2] Manipulation of the respiratory tract during endotracheal intubation is associated with increased circulating catecholamine leading to hemodynamic and cardiovascular responses resulting in increased heart rate, blood pressure, myocardial oxygen demand, arrhythmias, pulmonary artery, and capillary wedge pressure.[3]

The cardiovascular response is directly related to the force and duration of laryngoscopy. The response is transient occurring 30 sec after intubation & lasting for less than 10 minutes.[4]

Many prophylactic drugs & methods have been used to alleviate the cardiovascular response to laryngoscopy & intubation. Studies with alpha-2 adrenoreceptor agonists have demonstrated significant effects. Dexmedetomidine is a highly potent and selective alpha-2 adrenoceptor agonist, causes a dose-dependent decrease in blood pressure and heart rate, decreases the plasma catecholamine concentrations and reduces sympathetic nervous activity. Intravenous dexmedetomidine 1.0 µg/kg as slow infusion over a period of 10 minutes, 10

ISSN (O): 2687-5365; ISSN (P): 2753-6556

minutes before induction of anaesthesia attenuates the haemodynamic response to laryngoscopy and endotracheal intubation.

Magnesium acts as a calcium antagonist competitively binding to membrane channels and can modify the responses that are mediated by calcium, hence blocking the release of catecholamine stores and decreasing responses to adrenergic stimulations.[5-8] Magnesium also induces smooth muscle relaxation by reducing availability of calcium in the smooth muscles cytoplasm reducing its responsiveness to noradrenaline stimulation.[9,10]

The present study has been done to compare the effects of dexmedetomidine versus magnesium sulphate on hemodynamic parameters in patients undergoing laryngoscopy & intubation in elective surgery.

MATERIALS AND METHODS

This study was conducted in a tertiary care hospital after approval from Hospital Ethics Committee. 156 patients from ASA grade I & II, aged 18-60 year of either sex, posted for elective surgery (duration between 2-2.5 hrs) under general anaesthesia with endotracheal intubation were included in study. All patients underwent a complete preanesthetic check-up & written informed consent was taken. Patients who were allergic to study medication, had difficult airway, Hypertensive & cardiac disease patients, had intubation time > 20sec or > 1 attempt, morbidly obese (BMI > 30Kg/m2), Pregnant & nursing women and patients with Hepatic, renal, endocrine & psychiatric diseases were excluded from study.

The patients were kept fasted for 8 hrs. They received tablet alprazolam 0.25mg, tablet ranitidine 150 mg at 10 pm night prior to surgery & at 6 am on day of surgery.

Patients were randomly allocated in three groups: 1) group D – dexmedetomidine group (1 microgram/kg) 2) group M – magnesium sulphate (50 mg/kg) 3) group C- control (normal saline). Patients received study drugs through precoded syringes over 10 min before induction of general anaesthesia. All patients were hydrated with 6 ml/kg of Ringer Lactate before induction & then study drug infusion as per group was started. Patient's heart rate, systolic, diastolic, Mean Arterial Blood pressure, ECG, SPO2 and modified Ramsey sedation score were recorded just prior to study drug infusion (baseline values) and after drug infusion.

All patients were preoxygenated & then induction was done with Fentanyl citrate 2 mcg/kg, propofol 1.5 mg/kg over 45 seconds & vecuronium bromide 0.1 mg/kg intravenously. Patient was ventilated with O2 + N2O (50:50) for 4 min & then endotracheal intubation with a cuffed tube was performed by an experienced anesthesiologist. After conforming for bilateral equal air entry, normocapnic ventilation was started.

The following parameters: HR, NIBP (systolic, diastolic, mean BP), SPO2, ECG were recorded at:

T0- baseline T1- pre- induction T2- post- induction T3- before intubation T4- 1 min after intubation T5- 3 min after intubation T6- 5 min after intubation T7- 7 min after intubation T8- 10 min after intubation.

Maintenance of anaesthesia with O2+ N2O (40:60) + isoflurane(titrated) & vecuronium & fentanyl according to requirement. During the surgery any adverse event like bradycardia, tachycardia, or arrhythmia was recorded. Bradycardia was treated using injection atropine 0.6 mg i.v. & hypotension by normal saline & mephenteramine.

At the end of surgery neuromuscular blockade was reversed by inj. Neostigmine 50 mcg/kg & inj. Glycopyrrolate 10mcg/kg. Extubations were performed following extubation criteria. Patients were shifted to post anaesthetic recovery room & vitals or any other complications were monitored.

Our objective of study was to compare changes in haemodynamic parameters (HR, BP, ECG) with response to laryngoscopy.

With reference to previous study; we defined a clinically relevant difference in Haemodynamic with an effect size of 0.25 between any two groups. Using a two tailed alpha value (0.05) and a beta value (0.1), 52 patients per group were taken. The comparison of normally distributed continuous variables between the groups was performed using unpaired t-test or ANOVA. Nominal categorical data between the groups was compared using Chi-squared test or Fisher's exact test as appropriate. For all statistical tests, p value less than 0.05 will be taken to indicate a significant difference & p value less than 0.001 will be taken as highly significant.

RESULTS

Demographic data & duration of surgery between three groups were comparable. [Table 1]

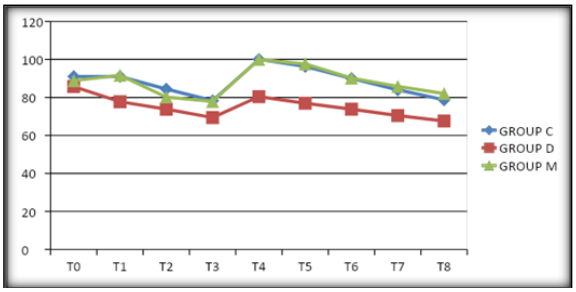

Figure 1: Comparison of Heart Rate Between Three Groups

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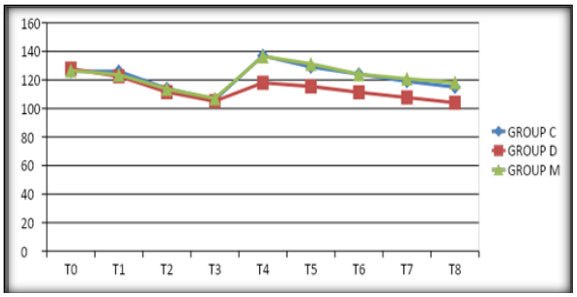

Figure 2: Comparison of SBP Between Groups

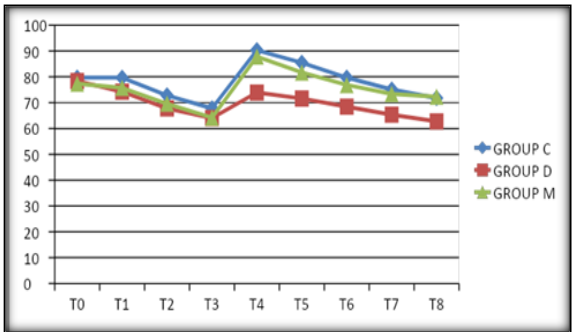

Figure 3: Comparison of DBP Between Groups

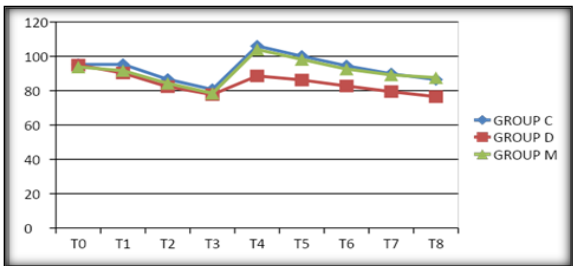

Figure 4: Comparison of MAP Between Groups

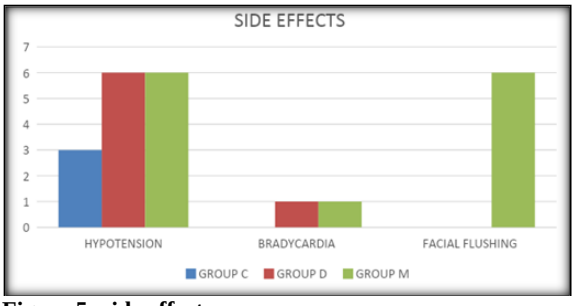

Figure 5: side effects

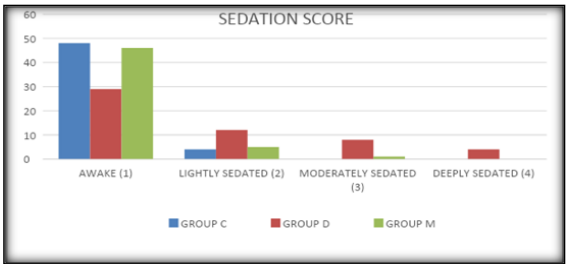

Figure 6: Sedation Score

Patients were sedated in both group D & M, but sedation was significantly more in group D. Also, sedation score was also higher in group D patients.

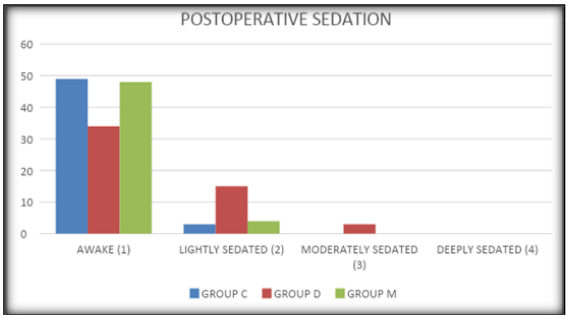

Figure 7: Post Operative Sedation

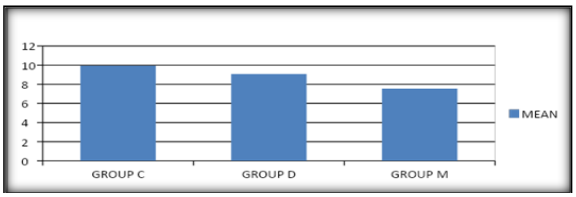

Figure 8: Requirement of Neuromuscular Blocking Agent

Table 1: Demographic Profile

Characteristics	Group D (n=52)	Group M (n=52)	GROUP C (n=52)	P value
Age (yrs)	37.02 + 10.41	38.85 + 13.21	39.35 + 11.96	0.33626
Sex (M:F)	21:31	26:26	29:23	0.284439
Weight	59.63 + 10.26	61.65 + 11.12	58.10 + 11.104	0.248
Height	164.73 + 3.946	163.40 + 7.179	162.75 +7.043	0.259
BMI	21.90 + 3.25	22.99 + 3.40	21.77 + 2.885	0.103
ASA (I:II)	49:3	46:6	47:5	0.577356
Duration of surgery (min)	127.38 + 12.49	128.77 + 13.41	126.69 + 14.72	0.730

Table 2: Comparison of Heart Rate between Three Groups

	GROUP C	GROUP D	GROUP M	p value between group C & D	p value between group C & M	p value between group D & M
T0	91 + 18	85.75 +18.4	88.81 +15.68	.0583	.220026	.181932
T1	91 +18	77.73 +18	91.69 +16.53	.000088	.459003	.000039
T2	84.4 +12.9	73.79 + 16.14	80.17 + 12.2	.000173	.044548	.01246
T3	78.3 +11.2	69.4 +14.14	77.9 +13.5	.000294	.440366	.001121

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T4	100 +16	80.4 +14.97	99.96 +16.64	.00001	.438758	<.00001
T5	96.3 +14.5	76.94 +14.65	97.63 +16.9	<.00001	.327212	<.00001
T6	90 +16	73.81 + 15.15	90.21 +14.69	<.00001	.454621	<.00001
T7	84 +15.8	70.44 +14.27	85.83 +12.92	<.00001	.264139	<.00001
T8	78.7 +13.6	67.6 +13.79	82.04 +13.11	.000037	.103904	<.00001

No significant difference was observed between groups at baseline heart rate.
After study drug infusion there was a significant fall in heart rate in group D as compared to other two groups but heart rate in group M increased at the same time.
After induction, there was fall in mean heart rate in all the groups with statistically significant fall in group D as compared to other two groups. Also, between group C & group M, there was significant fall in group M. After intubation, heart rate increased in all patients but the increase was more in patients of group C & M when compared to group D. There was statistically highly significant difference in heart rate between the group C & group D and group D & group M at 1, 3, 5, 7 and 10 min interval after intubation but there was non-significant difference in heart rate between group C & group M.

Table 3: Comparison of SBP Between Groups

	GROUP C	GROUP D	GROUP M	p value between group C & D	p value between group C & M	p value between group D & M
T0	126+ 11.9	127.9 + 12.81	126.6 + 15.91	.260736	.463903	.322656
T1	126+ 11.9	122.5 + 13.47	123.6 + 17.2	.062734	.170765	.361503
T2	114 +16	111.4 + 14.75	113.6 + 18	.187001	.442869	.247301
T3	106 + 17.5	105.1 + 15.83	107 + 16.34	.332349	.4426	.273766
T4	137 + 16.5	118 + 14.5	136.5 + 16.82	< .00001	.386707	< .00001
T5	129 + 14.1	115.4 + 12.83	131.2 + 17	< .00001	.271939	< .00001
eeeT6	124 + 12.9	111.3 + 13.62	124 + 15.52	< .00001	.494532	.000012
T7	119 + 12.3	107.7 + 13.4	120.8 + 17.11	< .00001	.299997	.000016
T8	115 + 12.81	104 + 12.61	118.2 + 15.56	< .00001	.192093	< .00001

Table 4: Comparison of DBP Between Groups

	GROUP C	GROUP D	GROUP M	p value between group C & D	p value between group C & M	p value between group D & M
T0	79.7+ 10.8	78.37+ 8.97	77.38+ 9.83	.242657	.125049	.298196
T1	79.7+ 10.8	74.25+ 9.99	75.71+ 10.03	.004259	.026107	.229122
T2	72.8+ 11.5	67.79+ 10.62	66.69 + 10.62	.010959	.002785	.299925
T3	67.8+ 11.4	64.06+ 9.58	64.17+ 10.8	.036268	.049135	.477077
T4	90.3+ 10.8	73.9+ 11.15	87.83+ 12.56	< .00001	.13921	< .00001
T5	85.46+ 9.95	71.6+ 9.81	81.67+ 17.34	< .00001	.087419	.00021
T6	79.7+10.6	68.46+ 10.36	76.85+ 12.84	< .00001	.108461	.000197
T7	75.1+9.96	65.35+ 9.51	73.37+ 12.93	< .00001	.223135	.000245
T8	71.8+ 10.3	62.75+ 8.88	72.3+ 12.9	< .00001	.420288	.000014

Table 5: Comparison of MAP Between Groups

	GROUP C	GROUP D	GROUP M	p value between group C & D	p value between group C & M	p value between group D & M
T0	95.3 + 10.7	94.89 + 9.13	93.8 + 10.91	.420673	.242933	.290976
T1	95.3 + 10.7	90.3 + 10.2	91.68 +11.28	.008839	.048742	.264239
T2	86.6 + 12.2	82.33 + 11.31	84.28 + 13.41	.033286	.177988	.21326
T3	80.7 + 12.4	77.72 + 11.07	78.44 + 11.92	.099613	.17217	.376559
T4	106 + 11.7	88.6 + 11.66	104 + 12.9	< .00001	.207588	< .00001
T5	100.1 +10.37	86.21 + 10.17	98.19 + 15.72	< .00001	.233827	< .00001
T6	94.5 + 10.6	82.74 + 10.67	92.56 + 12.82	< .00001	.206085	.000024
T7	89.8 + 9.98	79.47 + 10.1	89.18 + 13.38	< .00001	.391192.	.000031
T8	86.5 + 10.3	76.49 + 9.28	87.59 + 12.84	< .00001	.312202	< .00001

Preoperatively, there was no significant difference in SBP, DBP & MAP between 3 groups.
After study drug infusion there was fall in BP in both D & M groups & again after induction, there was fall in BP in all groups. Fall in DBP was significant in group D & M as compared to group C.
After intubation there was increase in SBP, DBP & MAP in all patients, but the increase was more in patients of group C & group M when compared group D. There was statistically highly significant difference in SBP the group C & group D and group D & group M at 1, 3, 5 ,7 and 10 min interval after intubation but there was non-significant difference in SBP between group C & group M at same time interval.

Table 6: Side Effects

SIDE EFFECTS	GROUP C		GROUP D		GROUP M		P VALUE
	N	%	n	%	N	%	
Hypotension	3/52	5.76	6/52	11.53	6/52	11.53	0.515

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Bradycardia	0/52	0	1/52	1.92	1/52	1.92	0.603
Facial flushing	0/52	0	0/52	0	6/52	11.53	0.002

All the groups were comparable with respect to side effect profile (hypotension). Bradycardia was seen in group D & M not in group C, but the difference was not significant.. Facial flushing which was significantly higher in group M.

Table 7: Sedation Score

	1		2		3		4	
	N	%	n	%	n	%	N	%
GROUP C	48	92.3	4	7.6	0	0	0	0
GROUP D	29	57.6	12	23.07	8	15.3	4	3.8
GROUP M	46	88.4	5	9.6	1	1.92	0	0

Table 8: P Value for Sedation Score

P value between groups		
C & D	D & M	C & M
0.0001	0.0001	0.371

Table 9: Post Operative Sedation Score

	1		2		3		4	
	N	%	n	%	n	%	N	%
GROUP C	49	94	3	5.7	0	0	0	0
GROUP D	34	65	15	28.8	3	5.7	0	0
GROUP M	48	92	4	7.6	0	0	0	0

Table 10: P Value for Postoperative Sedation Score

P value between groups		
C & D	D & M	C & M
0.0001	0.001	0.696

Post operatively patients were sedated in both groups D & M as compared to group C, but sedation was more significant in group D as compared to groups C & M.

Table 11: Requirement of Neuromuscular Blocking Agent

Groups	Mean	St. Deviation
Group C	9.28	1.24
Group D	9.08	1.25
Group M	7.54	1.22

Table 12: P Value for Requirement Of Neuromuscular Blocking Agent

P Value Between Groups		
C & D	D & M	C & M
0.388	0.0001	< 0.00001

Table 13: Recovery Characteristics Between Groups

Groups	Extubation time (min)		time to eye opening (min)		cooperation time (min)		orientation(min) (pt tell name & address)	
	Mean	St. Dev	Mean	St. Dev	Mean	St. Dev	Mean	St. Dev
GROUP C	5.24	0.98	6.22	0.96	7.71	0.78	8.80	0.89
GROUP D	5.26	0.97	6.21	0.81	7.77	0.9	8.89	0.91
GROUP M	5.29	1.11	6.28	1.58	7.79	1.38	9.15	0.97

Table 14: P Value for Recovery Characteristics

	Extubation time (min)	time to eye opening (min)	cooperation time (min)	orientation(min) (pt tell name & address)
P value	0.964	0.943	0.92	0.14

Recovery characteristics were similar in all 3 groups as shown by p value & graph. P values are insignificant for all the four criteria between three groups.

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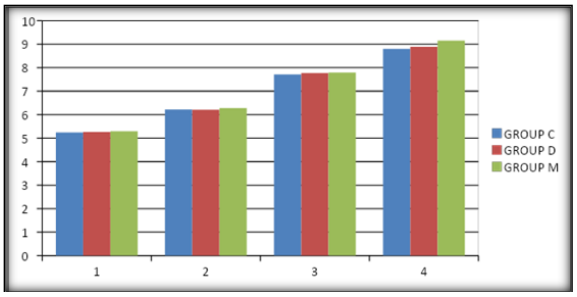

Figure 9: Recovery Characteristics Between Groups

DISCUSSION

Laryngoscopy and tracheal intubation are considered the most critical events during administration of general anaesthesia as they provoke transient but marked sympathoadrenal response manifesting as hypertension and tachycardia.

In the present study we compared the effect of dexmedetomidine 1 mcg/kg & magnesium sulphate 50 mg/kg on heart rate, systolic blood pressure, diastolic blood and mean blood pressure. In our study all groups were comparable regarding age, BMI and sex distribution. Our reason for studying the patients up to 60 years of age was that elderly patients more often are on drugs such as antidepressants, hypnotics and antihypertensives and also exhibit increased sensitivity to drugs.

Large induction doses of thiopentone sodium or propofol can largely increase the depth of anaesthesia thereby it may indirectly influence this haemodynamic response to laryngoscopy and intubation.[3,11] In our study, premedication with fentanyl at dose of 2 mcg/kg was given and fixed dose of propofol 1.5 mg/kg was used for induction in both the groups to avoid this bias.

Our results show that dexmedetomidine is a better drug as compared to magnesium sulphate for attenuation of laryngoscopy response.

Effect on heart rate

Heart rate is a major determinant of myocardial oxygen consumption. In the present study there was no statistically significant difference between the baseline heart rate of all the groups.

In the dexmedetomidine group the heart rate fell below baseline after its infusion, but in the magnesium sulphate group the heart rate increased above baseline after the magnesium sulphate infusion. The increase in heart rate post drug infusion is because patients are less sedated & more anxious in the magnesium sulphate group as compared to dexmedetomidine group. After induction, there was a fall in heart rate in all groups, with significant fall in the dexmedetomidine group. After intubation, increase in heart rate was not prominent in the dexmedetomidine group as compared to the control group & magnesium sulphate group. This shows dexmedetomidine attenuates the sympathoadrenal response to intubation effectively.

There was statistically highly significant difference in heart rate between the control group & dexmedetomidine group and dexmedetomidine group & magnesium sulphate group at 1, 3 , 5 ,7 and 10 min interval after intubation (p value < 0.01) but there was non-significant difference in heart rate between control group & magnesium sulphate group (p value > 0.05).

Our findings are comparable with following other studies:

Study done by Chaithanya K et al also shows the result that decrease in heart rate was more with dexmedetomidine compared to magnesium sulphate.[12] Decreases in heart rate values were statistically significant in the dexmedetomidine group compared to magnesium sulphate group ($p<0.005$), as shown in our study.

Mahajan L et al concluded in their study that on intergroup comparison, both group DS (dexmedetomidine group) and MS (magnesium sulphate group) had a highly significant ($P < 0.001$) fall in HR compared to NS (normal saline group) after study drug, but group DS showed a statistically highly significant attenuation of HR compared to MS up to 9 min.[13]

Ahmed A et al found that the use of dexmedetomidine in group D patients significantly decreased the changes in the mean heart rate either at the time of intubation (T1) or the following readings from T2 to T10[14]. Similarly, our study also shows that there is a fall in heart rate after giving drug in the dexmedetomidine group & there is less increase in heart rate in response to laryngoscopy as compare to magnesium sulphate & dexmedetomidine group.

Effects on BP

Baseline SBP, DBP & MAP were comparable between all groups. After study drug infusion there was fall in SBP, DBP & MAP in both dexmedetomidine group & magnesium sulphate group. After induction there was further fall in BP & there is significant fall in dexmedetomidine group as compared to magnesium sulphate group & control group. After intubation, we also observed an increase in blood pressure in all patients but the increase was more marked in patients of control group & magnesium sulphate group. The difference in the increase in systolic, diastolic and mean blood pressure at 1, 3-, 5-, 7- and 10-minutes post intubation interval was significant between the control groups & dexmedetomidine group and between dexmedetomidine group & magnesium sulphate group (p value < 0.05). This trend was attributed to the decrease in central sympathetic outflow in the dexmedetomidine group.

When dexmedetomidine premedication was compared to magnesium sulphate, a significant control of blood pressure and heart rate within a normal range with dexmedetomidine was observed in the present study.

Our findings are comparable with following other studies:

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Joshi C. et al show that mean fall in SBP, DBP & MAP in dexmedetomidine group immediately after intubation, at 2 minutes and 5 minutes after intubation was statistically highly significant (p=0.0001) compared to magnesium sulphate group.[15] Hence dexmedetomidine decreases the cardiac energy requirements better than magnesium sulphate at the above-mentioned doses.

Yildiz M et al and Varshali M K et al concluded that increase in blood pressure and heart rate were significantly less in the dexmedetomidine group.[16,17] Similarly, our study shows that there is more increase in heart rate & blood pressure in magnesium sulphate & control group as compared to dexmedetomidine group in response to laryngoscopy.

In our study dexmedetomidine is found to be superior than magnesium sulphate in attenuation of laryngoscopic response, which is different from study done by Chaithanya K et al which concluded that both Magnesium sulphate and dexmedetomidine controlled the systolic and diastolic blood pressure responses to laryngoscopy and endotracheal intubation effectively.[12] There was no statistically significant difference between both the drugs at 0, 1, 3, 5, and 10 minutes for systolic and diastolic blood pressures (p> 0.05)

Sedation

Sedation includes the whole spectrum of anxiety, amnesia and hypnosis.[18]

In our study, patients were less apprehensive and more sedated in the dexmedetomidine group compared to magnesium sulphate group as assessed by Modified Ramsay Sedation Score. Also, patients had higher sedation score in group D, both in preoperative period (after giving study drug infusion) & post operative period.

Side effects

Bradycardia was observed in one patient of the dexmedetomidine group and one patient in the magnesium sulphate group, which was managed with intravenous atropine 0.6 mg. Hypotension was seen in three patients of control group which was managed with fluid only, in six patients of dexmedetomidine group out of which four patients required mephenteramine & in six patients of magnesium sulphate group out of which two patients required mephenteramine. There was no significant difference observed between three groups for hypotension & bradycardia as compared by p value. Facial flushing was significantly higher in group M seen in six patients of magnesium sulphate group while infusion of magnesium sulphate. Infusion was stopped for some time & fluid given to patients & then infusion of drug again started at a slower rate.

Gomez-vazquez ME et al studied the clinical analgesic efficacy and side effects of dexmedetomidine and found bradycardia to be the most frequent adverse effect of this drug.[19] Study of Tandon N et al correlates with our study which shows that There were no significant differences in the prevalence of adverse events among the 3 groups.[20]

Requirement of neuromuscular blocking agents

Magnesium potentiates the action of non-depolarizing neuromuscular blockers by inhibiting the release of acetylcholine from the motor nerve terminal. It also decreases the sensitivity of post-junctional membrane and reduces the excitability of nerve fibre. As a result, reduced doses of non-depolarizing muscle relaxants are recommended when magnesium sulphate used.[21]

In our study also we found that there is a highly significant decrease in the requirement of neuromuscular blocking agent in group M as compared to other two groups (p value < 0.05).

Recovery characteristics

For analysing recovery characteristics, extubation time, time to eye opening, cooperation time & orientation time (when patient tells name & place of residence) all in minutes, were noted in all three groups & it was found that patients were comparable in all three groups.

Our study correlates with the study of Na HS et al, which shows that Intravenous magnesium sulphate reduces rocuronium requirements and postoperative analgesic consumption in children with CP.[22]

CONCLUSION

Dexmedetomidine is a better drug for attenuation of haemodynamic response (heart rate, SBP, DBP, MAP) to laryngoscopy & intubation, as compared to magnesium sulphate. Dexmedetomidine when given preoperatively produces more sedation which resembles normal sleep, as compared to magnesium sulphate.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556

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ISSN (O): 2687-5365; ISSN (P): 2753-6556